

REMARKS

Claims 1-17, 22-23, 25-29, 35, 37-40, 42-45 and 47-49 are pending in this application. Applicants have amended claims 1-6, 9, 12, 15 and 25 in this supplemental response.

On March 16, 2003, the Examiner contacted Applicants' representative regarding certain formatting objections to claims 1-6, 9, 12, 15 and 25. In response to these objections, Applicants submit this supplemental amendment to address the formatting issues raised by the Examiner. As no rejections or objections on the basis of patentability have been raised by the Examiner in this context, it remains that the pending claims, both before and after this amendment, comply with all statutory requirements relating to patentability. Applicants further submit that the scope of the claims has not been narrowed through this amendment.

In claims 1-6, 9, 12, 15 and 25, the Examiner objected to the wording and placement of the phrase "unsubstituted or substituted, straight chain or branched, hydrophobic, hydrophilic or fluorophilic." In this amendment, Applicants moved the phrase from its initial placement in the claim and reinserted the phrase as a separate "wherein clause" in a lower portion of the claim. This amendment should obviate the Examiner's concern regarding its initial placement. Furthermore, this amendment clarifies that the phrase relates to all constituents defined in the claim.

In claims 1-3, 6 and 9, the Examiner objected to the term "oxo." After reconsideration of the specification and the Examiner's original statutory objection to the term "=O" in the July 3, 2002 Office Action, the Examiner prefers that the claims recite the original term "=O." Applicants amend the claims back to their original format with regard to this claim term.

In claims 1, 2 and 6, the Examiner questioned the inclusion of the term "OOH" in the substituent list for moiety Z. As discussed with the Examiner in the March 16, 2003 telephone conference, this embodiment of moiety Z is chemically and sterically feasible as recited. Accordingly, Applicants did not amend this claim term in any manner.

In claims 6, 9 and 12, the Examiner objected to the second occurrence of the term "method." Per the Examiner's request, Applicants have deleted the second occurrence of this term in those method claims.

Additionally, Applicants have further amended claim 15 to remove a superfluous

recitation of the R<sub>1</sub> constituent.

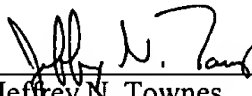
Applicants respectfully request reconsideration and allowance of this application in view of the above amendment and remarks.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned, "Version with markings to show changes made."

**Except** for issue fees payable under 37 C.F.R. §1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. §1.136(a)(3).

Respectfully submitted,

**MORGAN, LEWIS & BOCKIUS LLP**

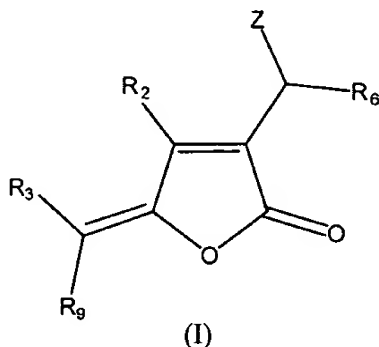
  
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Dated: March 18, 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. A compound according to formula (I):



wherein R<sub>6</sub> is H, OH, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl [whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic];

R<sub>2</sub> and R<sub>3</sub> are independently or both H or halogen;

R<sub>9</sub> is halogen;

Z is independently selected from R<sub>6</sub>, halogen, OOH, OC(O)R<sub>6</sub>,  $\underline{=O}$  [oxo], amine, azide, thiol, mercaptoalkyl, alkenyloxy, mercaptoalkenyl, aryloxy, mercaptoaryl, arylalkyloxy, mercaptoarylalkyl, SC(O)R<sub>6</sub>, OS(O)R<sub>6</sub>, OS(O)<sub>2</sub>R<sub>6</sub>, NHC(O)R<sub>6</sub> = NR<sub>4</sub> or NHR<sub>4</sub>; [and]

R<sub>4</sub> is OH, alkyl, alkoxy, poly(ethylene glycol), alkenyl, aryl or arylalkyl; and  
wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic;

provided that:

when R<sub>6</sub> is propyl, R<sub>2</sub> is Br, R<sub>3</sub> is H or Br and R<sub>9</sub> is Br, then Z is other than H, OC(O)CH<sub>3</sub> or OH;

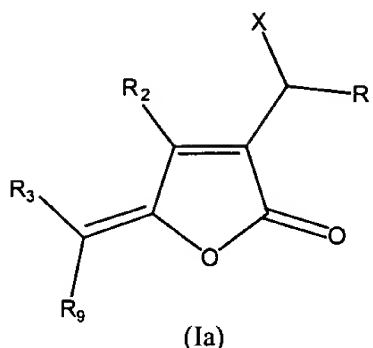
when R<sub>6</sub> is propyl, R<sub>2</sub> is Br, R<sub>3</sub> is H and R is I, then Z is other than OC(O)CH<sub>3</sub> or OH;

when R<sub>6</sub> is propyl, R<sub>2</sub> is Br, R<sub>3</sub> is H and R is Cl, then Z is other than OH;

when R<sub>6</sub> is propyl, R<sub>2</sub> is H, R<sub>3</sub> and R are Br, then Z is other than H; and

when R<sub>6</sub> is propyl, R<sub>2</sub> is Br, R<sub>9</sub> is Cl and Z is H, then R<sub>3</sub> is other than Cl.

2. A compound according to formula (Ia):



wherein R<sub>1</sub> is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl [whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic];

X is a halogen, OH, OOH, OC(O)R<sub>1</sub> or =O [oxo];

R<sub>2</sub> and R<sub>3</sub> are independently or both hydrogen or halogen; [and]

R<sub>9</sub> is halogen; and

wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic;

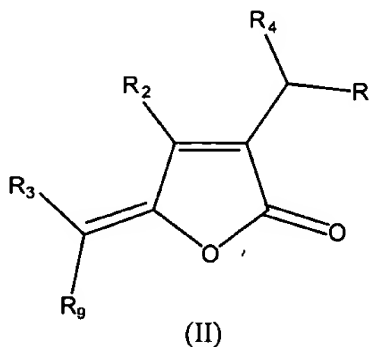
provided that:

when R<sub>1</sub> is propyl, R<sub>2</sub> is Br, R<sub>3</sub> is H or Br and R<sub>9</sub> is Br, then X is other than OC(O)CH<sub>3</sub> or OH;

when R<sub>1</sub> is propyl, R<sub>2</sub> is Br, R<sub>3</sub> is H and R<sub>9</sub> is I, then X is other than OC(O)CH<sub>3</sub> or OH; and

when R<sub>1</sub> is propyl, R<sub>2</sub> is Br, R<sub>3</sub> is H, R<sub>9</sub> is Cl, then X is other than OH.

3. A compound according to formula (II):



wherein  $R_1$  is hydrogen [, unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic] alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl;

$R_2$  and  $R_3$  are independently or both hydrogen or halogen;

$R_9$  is halogen; [and]

$R_4$  is selected from halogen, amine, azide, hydroxyl, thiol, or hydrophobic, hydrophilic or fluorophilic alkyl, alkoxy, mercaptoalkylalkenyloxy, mercaptoalkenyl, aryloxy, mercaptoaryl, arylalkyloxy, mercaptoarylalkyl,  $OC(O)R_1$ ,  $SC(O)R_1$ ,  $OS(O)R_1$ ,  $OS(O)_2R_1$ ,  $NHC(O)R_1$ ,  $OC(O)NHR_1$ , or  $=O$  [oxo]; and

wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic;

provided that:

when  $R_4$  is propyl,  $R_2$  is Br,  $R_3$  is H or Br, and  $R$  is Br, then  $R_1$  is other than H,  $OC(O)CH_3$  or OH;

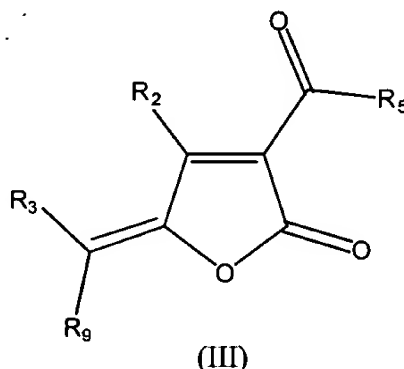
when  $R_4$  is propyl,  $R_2$  is Br,  $R_3$  is H,  $R_9$  is I, then  $R_1$  is other than  $OC(O)CH_3$ , or OH;

when  $R_4$  is propyl,  $R_2$  is Br,  $R_3$  is H,  $R_9$  is Cl, then  $R_1$  is other than OH;

when  $R_4$  is propyl,  $R_2$  is H,  $R_3$  and  $R_9$  are Br, then  $R_1$  is other than H; and

when  $R_4$  is propyl,  $R_2$  is Br,  $R_3$  and  $R_9$  are Cl, then  $R_1$  is other than H.

4. A compound according to formula (III):



wherein  $R_2$  and  $R_3$  are independently or both hydrogen or halogen;

$R_5$  is OH or the same as  $R_1$ ;

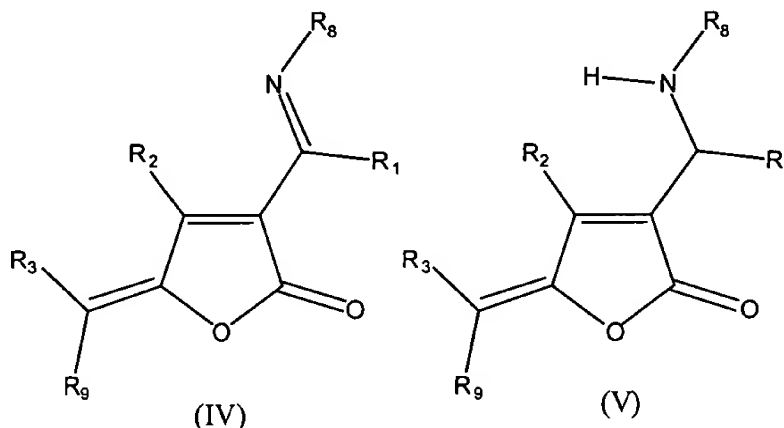
$R_9$  is halogen; [and]

$R_1$  is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl; and [whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or

fluorophilic}.

wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic.

5. A compound according to formula (IV) or (V):



wherein R<sub>1</sub> is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl [whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic];

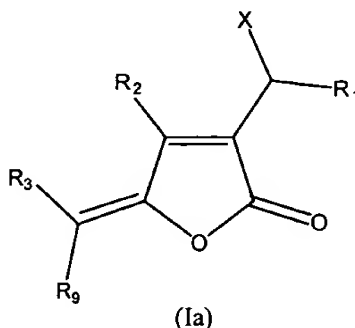
R<sub>2</sub> and R<sub>3</sub> are independently or both hydrogen or halogen;

R<sub>9</sub> is halogen; [and]

R<sub>8</sub> is OH, NHR<sub>1</sub>, NHC(X)NH<sub>2</sub>, NHC(X)NHR<sub>1</sub> or R<sub>1</sub> where X is O, S or NR<sub>1</sub>; and

wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic.

6. A method for forming a compound of formula (Ia), [the method] comprising reacting a fimbrolide with a halogenating agent and/or an oxygenating agent to form the compound of formula (Ia):



wherein  $R_1$  is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl [whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic];

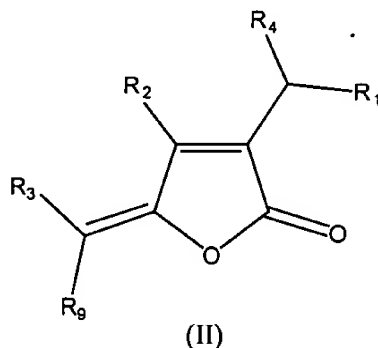
$X$  is a halogen, OH, OOH,  $OC(O)R_1$  or  $\equiv O$  [oxo];

$R_2$  and  $R_3$  are independently or both hydrogen or halogen; [and]

$R_9$  is halogen; and

wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic.

9. A method for forming a compound of formula II, [the method] comprising displacing and/or functionalizing a halogen or oxygen substituent in the side chain of a fimbrolide compound by treating the fimbrolide compound with a nucleophile or an electrophile to form the compound of formula (II):



wherein  $R_1$  is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl [whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic];

$R_2$  and  $R_3$  are independently or both hydrogen or halogen;

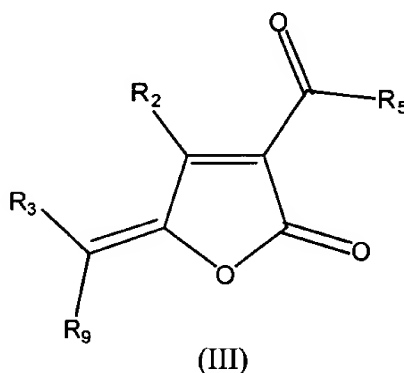
$R_9$  is halogen; [and]

$R_4$  is selected from halogen, amine, azide, hydroxyl, thiol, or any hydrophobic, hydrophilic or fluorophilic alkyl, alkoxy, mercaptoalkyl, alkenyloxy, mercaptoalkenyl, aryloxy, mercaptoaryl, arylalkyloxy, mercaptoarylalkyl,  $OC(O)R_1$ ,  $SC(O)R_1$ ,  $OS(O)R_1$ ,  $OS(O)_2R_1$ ,  $NHC(O)R_1$ ,  $OC(O)NHR_1$ , or  $\equiv O$  [oxo,]; and

wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic;

provided that when  $R_4$  is propyl,  $R_2$  is Br,  $R_3$  and  $R_9$  are Cl, then  $R_1$  is other than H.

12. A method for forming a compound of formula (III), [the method] comprising reacting an hydroxyl substituent in the side chain of a fimbrolide with an oxidising agent to form the compound in accordance with formula (III):



wherein  $R_2$  and  $R_3$  are independently or both hydrogen or halogen;

$R_5$  is OH or the same as  $R_1$ ;

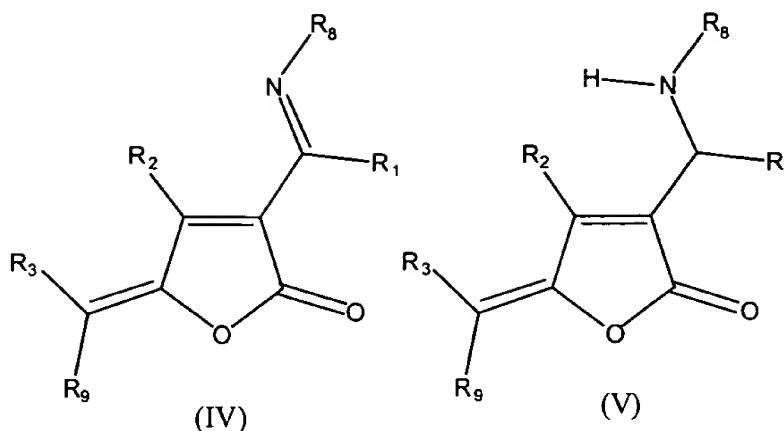
$R_9$  is halogen; [and]

$R_1$  is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl [whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic]; and wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic.

15. A method for forming a compound of formula (IV) or (V), comprising reacting an aldehyde or ketone substituent in the side chain  $--C(O)R_5$  of compound (III) with an amine to form a compound of formula (IV) or (V),

wherein formula (IV) and (V) are represented by:





wherein  $R_1$  is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl [whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic];

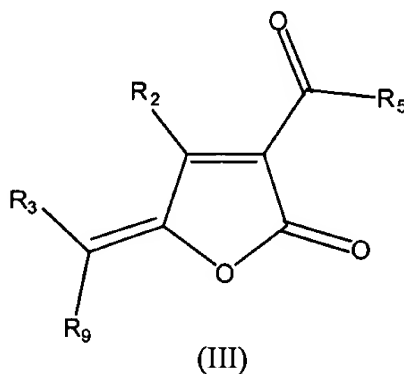
$R_2$  and  $R_3$  are independently or both hydrogen or halogen;

$R_9$  is halogen; [and]

$R_8$  is OH,  $NHR_1$ ,  $NHC(X)NH_2$ ,  $NHC(X)NHR_1$  or  $R_1$  where X is O, S or  $NR_1$ ; and

wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic;

and wherein formula (III) is represented by:



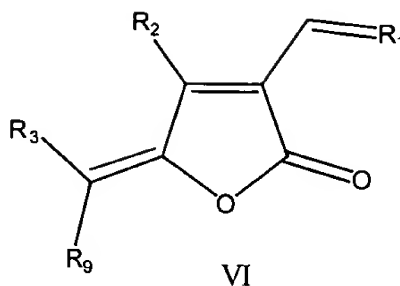
wherein  $R_2$  and  $R_3$  are independently or both hydrogen or halogen;

$R_5$  is OH or the same as  $R_1$ ; and

$R_9$  is halogen[; and]

[ $R_1$  is hydrogen, alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic].

25. A compound of formula (VI):



wherein  $R_1$  is alkyl, alkoxy, oxoalkyl, alkenyl, aryl or arylalkyl [whether unsubstituted or substituted, straight chain or branched chain, hydrophobic, hydrophilic or fluorophilic];

$R_2$  and  $R_3$  are independently or both hydrogen or halogen; [and]

$R_9$  is halogen; and

wherein each constituent can be substituted or unsubstituted, straight chain or branched chain, and hydrophobic, hydrophilic or fluorophilic.